

Atty Dkt 7010-0018  
OPF 18.20  
PATENT

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on 26-NOVEMBER-2001.

11/26/01  
Date

[Signature]  
Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

O'Connor et al.

Serial No.: 09/922,218

Group Art Unit: Unassigned

Filing Date: August 3, 2001

Examiner: Unassigned

Title: HYDROGEL PARTICLE FORMULATIONS

TRANSMITTAL LETTER

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Transmitted herewith for filing is an Information Disclosure Statement, including a Form PTO-1449 and copies of the cited references. No fee is required.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16, 1.17 and 1.21 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 18-1648.

Respectfully submitted,

Date: 11/26/01

By: [Signature]  
Roberta L. Robins  
Registration No. 33,208

ROBINS & PASTERNAK LLP  
90 Middlefield Road, Suite 200  
Menlo Park, CA 94025  
Telephone: (650) 325-7812  
Facsimile: (650) 325-7823



Atty Dkt 7010-0018  
OPF 18.20  
PATENT

#f

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on 26 NOVEMBER 2001.

11/26/01  
Date

[Signature]  
Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

O'Connor et al.

Serial No.: 09/922,218

Group Art Unit: Unassigned

Filing Date: August 3, 2001

Examiner: Unassigned

Title: HYDROGEL PARTICLE FORMULATIONS

**INFORMATION DISCLOSURE STATEMENT  
UNDER 37 C.F.R. § 1.97**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

The information listed below may be material to the examination of the above-identified application. Copies of the information and completed PTO-1449 forms are submitted herewith. The Examiner is respectfully requested to make this information of official record in the application. The information includes:

United States Patent No. 4,853,226 issued August 1, 1989 to Machida et al.;  
United States Patent No. 4,925,677 issued May 15, 1990 to Feijen;  
United States Patent No. 4,978,069 issued December 18, 1990 to Anderson et al.;  
United States Patent No. 4,994,276, issued February 19, 1991 to Baichwal et al.;  
United States Patent No. 5,041,292 issued August 20, 1991 to Feijen;  
United States Patent No. 5,053,332 issued October 1, 1991 to Cook et al.;  
United States Patent No. 5,700,459 issued Dec. 23, 1997 to Krone et al.;  
International Publication No. WO 94/09819 published May 11, 1994;  
International Publication No. WO 95/13798 published May 26, 1995;

International Publication No. WO 96/12513 published May 2, 1996;  
International Publication No. WO 96/20022 published July 4, 1996;  
International Publication No. WO 97/48485 published December 24, 1997;  
International Publication No. WO 98/10750 published March 19, 1998;  
International Publication No. WO 00/15263 published March 23, 2000;  
European Publication No. 0 357 401 published March 7, 1990;  
Great Britain Publication No. 2 245 831 published January 15, 1992;  
Aasted, Bent, "Highly purified Agarose as Stacking Gel in Sodium Dodecyl Sulphate/Polyacrylamide-Gel Electrophoresis," *Biochem. J.* 189:183-184 (1980);  
Albright et al., "Diet, Apoptosis, and Carcinogenesis," *Adv. Exper. Med. And Biol.* 422:92-107 (1997);  
Cadic-Amadeuf et al., "Inflammatory Reaction Induced by Agarose Implants Reduced by Adding Adrenal Cells to the Polymer," *ASAIO Journal* 38(3);M386-M389 (1992);  
Anderson and Hagel, "Some Properties and Applications of Superose 6B," *Analytical Biochemistry* 141:461-465 (1984);  
Andrasko, Jan, "Water in Agarose Gels Studied by Nuclear Magnetic Resonance Relaxation in the Rotating Frame," *Biophys. Journal* 15(12):1235-1243 (1975);  
Arndt, E.R. and Stevens, E. S., "Anhydro Sugar and Linkage Contributions to Circular Dichroism of Agarose and Carrageenan, With Conformational Implications," 303:73-78 (1997);  
Arnott et al., "The Agarose Double Helix and Its Function in Agarose Gel Structure," *J. Mol. Biol.* 90:269-284 (1975);  
Arshady, Reza, "Microspheres for Biomedical Applications: Preparation of Reactive and Labelled Microspheres," *Biomaterials* 14(1):5-15 (1993);  
Artursson et al., "Biodegradable Microspheres, 1. Duration of Action of Dextranase Entrapped in Polyacrylstarch Microparticles *in Vivo*," *The Journal of Pharmacology and Experimental Therapeutics* 231(3):705-712 (1986);  
Ауцук et al., "Method of Obtaining Agarose from Agar-Agur," *Lab Delo* 6:370-371 (1976);

- Bourrillos, et al., "An Improved Method for Preparing Agarose," *Biochim. Biophys. Acta* 111:334-336 (1965);
- Brogren, Carl-Henrik, "Brownian Motion and Electrophoretic Transport in Agarose Gels Studied by Epifluorescence Microscopy and Single Particle Tracking Analysis," *J. Phys. Chem. B.* 101:5659-5663 (1997);
- Bulone et al., "Mesoscopic Gels at Low Agarose Concentration: Perturbation Effects of Ethanol," *Biophysical Journal* 72:388-394 (1997);
- Muro-Cacho, Carlos A., "In Situ PCR: Overview of Procedures and Applications," *Frontiers in Bioscience* 2:15-19 (1997);
- Chan et al., "An Inexpensive Solid Medium for Obtaining Colony-Forming Units of Oral Spirochetes," *Oral Microbiology Immunology* 12:372-376 (1997);
- Coppi et al., "Polysaccharide Film-Coating Process for Freely Swellable Hydrogels," *Pharmaceutical Development and Technology* 3(3):347-353 (1998);
- Cowan, D. E., "Thermophilic Proteins: stability and Function in Aqueous and Organic Solvents," *Comp. Biochem. Physiol.* 118A(3):429-438 (1997);
- Davies et al., "Improved Manufacture and Application of an Agarose Magnetizable Solid-Phase Support," *Appl. Biochem. Biotechnol.* 68(1-2):95-112 (1997);
- Davis, S.S. and Illum, L., "Polymeric Microspheres as Drug Carriers," *Biomaterials* 9(1):111-115 (1988);
- de Koning et al., "Crosslinked Agarose Encapsulated Sorbents Resistant to Steam Sterilization. Preparation and Mechanical Properties," *J. Biomed. Mat. Res.* 18:1-13 (1984);
- Draye et al., "In vitro Characteristics of bioactive Molecules from Dextran Dialdehyde Cross-Linked Gelatin Hydrogel Films," *Biomaterials* 19:99-107 (1998);
- Eppstein et al., "Alternative Delivery Systems for Peptides and Proteins As Drugs," *CRC Critical Reviews in Therapeutic Drug Carrier System* 5(2):99-139 (1998);
- Gehrke et al., "Enhanced Loading and Activity Retention of Bioactive Proteins in Hydrogel Delivery Systems," *Journal of Controlled Release* 55:21-33 (1998);
- Gombotz, W. and Pettit, DK., "Biodegradable Polymers for Protein and Peptide Drug Delivery," *Bioconjugate Chem.* 6(4):332-351 (1995);

- Gribnau et al., "Microscopic Observations on Commercial Sepharose Deviations From Normal Bead-Structure," *FEBS Letters* 57(3):301-303 (1975);
- Gustavsson et al., "Superporous Agarose Beads as a Hydrophobic Interaction Chromatography Support," *Journal of Chromatography A* 830:275-284 (1999);
- Gustavsson et al., "Continuous Superporous Agarose Beds for Chromatography and Electrophoresis," *Journal of Chromatography A* 832:29-39 (1999);
- Häglund et al., "Dissolution Controlled Drug Release From Agarose Beads," *Drug Development and Industrial Pharmacy* 20(6):947-959 (1994);
- Hjertén, S. and Liao, J., "High-Performance Liquid Chromatography of Proteins on Compressed, Non-Porous Agarose Beads," *Journal of Chromatography* 457:165-174 (1988);
- Holloway et al., "Agarose-Encapsulated Adsorbents," *The International Journal of Artificial Organs* 2(1):81-86 (1979);
- Howe, F.A., "Relaxation times in Paramagnetically Doped Agarose Gels as a Function of Temperature and Ion Concentration," *Magnetic Resonance Imaging* 6:263-270 (1988);
- Ito et al., "Quantitative Prediction of *in Vitro* Drug Clearance and Drug Interactions from *in Vitro* data on Metabolism, Together with Binding and Transport," *Annu. Rev. Pharmacol. Toxicol.* 38:461-499 (1998);
- Frank-Kamenetskii, M., "A Simple Solution to the Stability of the Double Helix?," *Nature* 324:p.305 (1986);
- Kanke et al., "Clearance of <sup>141</sup> Ce-Labeled Microspheres from Blood and Distribution in Specific Organs Following Intravenous and Intraarterial Administration in Beagle Dogs," *Journal of Pharmaceutical Sciences* 69(7):755-762 (1980);
- Kikuchi et al., "Effect of Ca<sup>2+</sup> -Alginate Gel Dissolution on Release of Dextran with Different Molecular Weights," *Journal of Controlled Release* 58:21-28 (1999);
- Kim et al., "Hydrogels: Swelling, Drug Loading, and Release," *Pharmaceutical Research* 9(3):283-290 (1992);

Jani, G.K., and Gohel, M.C., "Effects of Selected formulation Parameters on the Entrapment of Diclofenac Sodium in Ethyl Cellulose Microspheres," *Journal of Controlled Release* 43:245-250 (1997);

Kuijpers et al., "Controlled Delivery of Antibacterial Proteins From Biodegradable Matrices," *Journal of Controlled Release* 53:235-247 (1998);

Li et al., "High-Performance Liquid Chromatography of Proteins on Deformed NonPorous Agarose Beads. Affinity Chromatography of Dehydrogenases Based on Cibacron Blue-Derivatized Agarose," *Preparative Biochemistry* 20(2):107-121 (1990);

Lösgen et al., "Large Agarose Beads for Extracorporeal Detoxification System," *Biomat. Med. Dev. Art. Org.* 6(2):151-173 (1978);

Lundberg, P. and Kuchel, P.W., "Diffusion of Solutes in Agarose and Alginate Gels: <sup>1</sup>H and <sup>23</sup>Na PFGSE and <sup>23</sup>Na TQF NMR Studies," *Mag. Res. Med.* 37(1):44-52 (1997);

Maaloum et al., "Agarose Gel Structure Using Atomic Force Microscopy: Gel concentration and Ionic Strength Effects," *Electrophoresis* 19:1606-1610 (1998);

Margel, S., "Agarose-Polyaldehyde Microsphere Beads: Synthesis and Biomedical Applications," *Applied Biochemistry and Biotechnology* 8:523-539 (1983);

Margel, S., and Offarim, M., "Novel Effective Immunoabsorbents Based on Agarose-Polyaldehyde Microsphere Beads: Synthesis and Affinity Chromatography," *Analytical Biochemistry* 128:342-350 (1983);

McNeil, M.E. and Graham N. G., "Properties Controlling the Diffusion and Release of Water-Soluble Solutes from Poly(Ethylene Oxide) Hydrogels: 3.Device Geometry," *J. Biomater. Sci. Polymer Edn.* 7(11):937-951 (1996);

Mitsuiki et al., "Determination of Molecular Weight of Agars and Effect of the Molecular Weight on the Glass Transition," *J. Agric. Food Chem.* 47:473-478 (1999);

Moussaoui et al., "Diffusion of Proteins in Sepharose C1-B Gels," *Journal of Chromatography* 591:115-120 (1992);

Munjeri et al., "Hydrogel Beads Based on Amidated Pectins for Colon-Specific Drug Delivery: The Role of Chitosan in Modifying Drug Release," *Journal of Controlled Release* 46:273-278 (1997);

Munjeri et al., "An Investigation into the Suitability of Amidated Pectin Hydrogel Beads as a Delivery Matrix for Chloroquine," *Journal of Pharmaceutical Sciences* 87(8):905-908 (1998);

Nakano et al., "Agarose-Encapsulated Adsorbent Beads for Direct Hemoperfusion: Preparation and *in Vitro* Evaluation," *Chem. Pharm. Bul.* 342:2591- 2598 (1986);

Okada et al., "Medical Application of Microencapsulating Hybridoma Cells in Agarose Microbeads "Cytomedicine": Therapeutic Effect on igG1 Plasmacytosis and Mesangio-Proliferative Glomerulonephritis in the Interleukin 6 Transgenic Mouse," *Journal of Controlled Release* 44:195-200 (1997);

Okada, H. and Toguchi, H., "Biodegradable Microspheres in Drug Delivery," *Critical Reviews in Therapeutic Drug Carrier Systems* 12(1):1-99 (1995);

Patil, R. and Speaker, T.J., "Water-Based Microsphere Delivery System for Proteins," *Journal of Pharmaceutical Sciences* 89(1):9-15 (2000);

Patil et al., "Macroporous Poly(Sucrose Acrylate) Hydrogel for Controlled Release of Macromolecules," *Biomaterials* 17(24):2343-2350 (1996);

Pernodet et al., "Pore Size of Agarose Gels by Atomic Force Microscopy," *Electrophoresis* 18:55-58 (1997);

Polson et al., "Preparation of Agarose with Low Net Negative Charge Density Using an Expensive Anion Exchanger," *Preparative Biochemistry* 16(4):309-319 (1986);

Polson et al., "Agarose: A Possible Universal Gel Exclusion Agent," *Preparative Biochemistry* 14(2):173-179 (1984);

Ramzi et al., "Structure-Properties Relation for Agarose Thermoeversible Gels in Binary Solvents," *Macromolecules* 31:6106-6111 (1998);

Rees, D. A., "Structure Confirmation and Mechanism in the Formation of Polysaccharide Gels and Networks," *Advances in Carbohydr. Chem Biochem.* 24:3+7-332 (1969);

Schroeder et al., "Distribution of radiolabeled Subvision Microspheres After Intravenous Administration to Beagle Dogs," *J. Pharm. Sci.* 67(4):504-509 (1978);

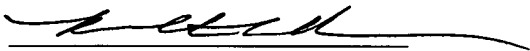
- Schroeder et al., "Physiological Effect of Subvision Microspheres Administered to Beagle Dogs," *J. Pharm. Sci.* 67(4):508-513 (1978);
- Sideman et al., "Tailor-Made Agarose-Based Reactive Beads for Hemoperfusion and Plasma Perfusion," *Applied Biochemistry Biotechnology* 10:167-182 (1984);
- Sjöbert et al., "How Interactions Between Drugs and Agaros-Carrageenan Hydrogels Influence the Simultaneous Transport of Drugs," *Journal of Controlled Release* 59:391-400 (1999);
- Stellwagen, J. and Stellwagen, N.C., "The Effect of Gel Structure on Matrix Orientation," *Electrophoresis* 13:595-600 (1992);
- Stenekes, R.J.H. and Hennik, W.E., "Equilibrium Water Content of Microspheres Based on Cross-Linked Dextran," *International Journal of Pharmaceutics* 189:131-135 (1999);
- Tanaka, Toyochi, *Gels* 124-138;
- Thano et al., "Biodegradable Indium-111 Labeled Microspheres for *in Vivo* Evaluation of Distribution and Elimination," *Pharmaceutical Research* 12(12):2060-2064 (1995);
- Vanbever et al., "Formulation and Physical Characterization of Large Porous Particles for Inhalation," 16(11):1735-1741 (1999);
- Waki, S. and Harvey, J.D., "Study of Agarose Gels by Electro Microscopy of Freeze-Fractured Surfaces," *Biopolymers* 21:1909-1926 (1982);
- Walker et al., "Preparation of Agarose Gels as Reference Substances for NMR Relaxation Time Measurement," *Magnetic Resonance Imaging* 6:215-222 (1988);
- Wang N. and Wu, X.S., "Preparation and Characterization of Agarose Hydrogel Nanoparticles for Protein and Peptide Drug Delivery," *Pharmaceutical Development and Technology* 2(2):135-142 (1997); and
- White, K.N., *Tanpakushitsu Kakusan Koso* 221(13):1431-1436 (1977).

This Information Disclosure Statement under 37 CFR § 1.97 is not to be construed as a representation that: (i) a complete search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the information,

protocols, results and the like reported by third parties are accurate or enabling; or (iv) the above information constitutes prior art to the subject invention.

Respectfully submitted,

Date: 11/26/01

By:   
Roberta L. Robins  
Registration No. 33,208

ROBINS & PASTERNAK LLP  
90 Middlefield Road, Suite 200  
Menlo Park, CA 94025  
Telephone: 650-325-7812  
Facsimile: 650-325-7823